Atty. Dkt. No. 039386-0307
(PF-0544USN)

REMARKS

The detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented in the foregoing section above, with an appropriate defined status identifier for each claim. Claims 21-24, 30, and 36-38 are cancelled herein. Claims 25-29, 31, 32, 34, 35, 39, and 40 are amended herein. Upon entry of the amendments herein, claims 25-29, 31, 32-35, 39, and 40 are pending in this application.

The claim amendments herein do not contain new matter. As required by the Examiner on page 7, item 3 of the Official Action, the amendments to claims 25, 26, 28, 29, 31, 35, and 39 excise recitation drawn to non-elected subject matter. The amendment to claims 26, 27, 28, 31, 32, 34, 39, and 40 clarifies what Applicants regard as the invention.

For the reasons provided above, the claim amendments herein do not contain new matter. Applicants respectfully request reconsideration of the present application in view of the foregoing amendments and in view of the arguments that follow.

ARGUMENTS

Priority

The present application is a U.S. national stage entry of PCT/US99/14711 that claims priority to U.S. Provisional Applications 60/091,177 (filed June 30, 1998) and 60/155,241 (filed July 16, 1998). The Patent Office alleges that "none of the priority documents show support for the polynucleotide sequence SEQ.ID.NO: 11 with 3184 nucleotides..." [Official Action at page 8, item 5]. Applicants respectfully disagree and direct the Patent Office's attention to SEQ ID NO: 3, consisting of 3184 nucleotides, listed in the Sequence Listings on pages 2-3 of U.S. Provisional Application 60/155,241. A complete paper copy of the Sequence Listings submitted in the filing of U.S. Provisional Application 60/155,241 is provided herein as Exhibit A.

35 U.S.C. §101 and §112, first paragraph- Utility

Claims 23-29 and 31 are rejected under 35 U.S.C. §101 and §112, first paragraph for alleged lack of a specific asserted or a well-established utility. Specifically, the Patent Office alleges that "because the function of the SEQ. ID NO: 11 is not disclosed, the credibility of the asserted utilities... cannot be assessed" [Official Action, Item 8 at page 11, paragraph 1].

Polynucleotides of the present invention encode novel human oxidoreductase proteins. As amended herein, independent claim 31 is presently drawn to an isolated polynucleotide selected from the group consisting of a polynucleotide comprising a polynucleotide sequence of SEQ ID NO: 11, a polynucleotide comprising a polynucleotide sequence having at least 90% sequence identity to SEQ ID NO: 11, polynucleotides complementary thereto, and RNA equivalents thereof. Applicants respectfully disagree with the Patent Office's allegations for the reasons provided below.

A. The Specification Sufficiently Describes the Relationship of Inventive Polypeptides to Known Proteins

The Patent Office alleges that "the specification does not provide any disclosure as to how the polynucleotide encoding the claimed polypeptide relate to any known proteins" [Official Action Item 8 at page 9, paragraph 3]. Applicants respectfully assert that the specification provides sufficient disclosure of the relationship of the inventive polypeptide to known oxidoreductase proteins, such as cytochrome b5/desaturase fusion protein.

The specification explicitly describes the inventive polypeptide as sharing "**chemical and structural similarity** with sunflower cytochrome b5/desaturase fusion protein" [emphasis added in bold, Specification at page 16, lines 30-31]. In fact, the Patent Office admits that inventive polypeptides "share 23% identity with sunflower cytochrome b5/desaturase fusion protein" [Official Action, Item 8 at page 9, paragraph 3].

In addition to describing shared sequence similarities, the specification further provides description of shared structural similarities between the inventive polypeptides and sunflower cytochrome b5/desaturase fusion protein. For example, the specification states that inventive polypeptides, such as HORP-5 (corresponding to SEQ ID NO: 5 of the present application) share the following exemplary structural features with sunflower cytochrome b5/desaturase fusion protein:

1. "potential heme-binding site, located at H53PGG in HORP-5,"
2. "seven cytochrome b5 superfamily invariant residues, located at H53, P54, G55, G56, F72 and H76 in HORP-5,"
3. "nine cytochrome b5 superfamily conserved residues, located at V43, Y44, N45, T47, W49, D67, T69, L89, and G92 in HORP-5,"
4. "similar amino acid residues at four cytochrome b5 superfamily conserved sites, located at I26, L37, S50, and I60 in HORP," and

5. "three potential desaturase histidine boxes; located at H180DYGH, H217FQHH, and Q3821EHH in HORP-5" [Specification at page 16, line 33- page 17, line 6].

Additional description in the specification regarding the relationship of inventive polypeptides to known protein is provided, for example, in Table 2 at page 60. Table 2 lists signature sequences, such as sequences pertaining to transmembrane domains, heme-binding domains, and cytochrome b5 signature sequences, of an exemplary inventive polypeptide, SEQ ID NO: 5.

Therefore, contrary to the Examiner's allegation, the specification does indeed provide sufficient disclosure as to how the inventive polypeptides relate to known proteins, such as cytochrome b5/desaturase fusion protein, as evidenced, in part, by the exemplary citations discussed above.

B. The Specification Describes Biological Properties of Invention Polynucleotides

The Patent Office further alleges that "the specification does not disclose the expression of this protein in any tissue of a given subject" [Official Action, Item 8 at page 9, paragraph 3]. As a first point, the presently claimed invention is drawn to polynucleotides, not polypeptides. Applicants respectfully assert that the specification provides sufficient disclosure regarding the biological properties, such as tissue expression, of invention polynucleotides.

The specification describes RNA expression of invention polynucleotides in various types of tissue libraries. For instance, the specification states:

> Northern analysis shows the expression of SEQ ID NO:11 in various libraries, at least 59% of which are immortalized or cancerous, at least 26% of which involve immune response, and at least 23% of which are fetal or proliferating cell or tissues. Of particular note is the expression of SEQ ID NO:11 in male and female reproductive, nervous, cardiovascular, and endocrine

tissues [emphasis added in bold, Specification, page 17, lines 6-12].

Additional description regarding tissue expression of invention polynucleotides is provided in Table 3 of the specification at page 61. As explicitly stated in the specification on page 8, lines 1-2, "the second column [of Table 3] lists the tissue expression of HORP and fraction of total tissue which express" SEQ ID NO: 11. Therefore, contrary to the Examiner's allegation, the specification does indeed provide sufficient disclosure regarding expression of invention polynucleotides.

Applicants respectfully assert that specification provides specific, well-established, and credible utility for the claimed invention. As evidenced by the exemplary citations provided above, the specification explicitly describes chemical, structural, and biological properties of the claimed invention. For these reasons, withdrawal of the rejection of claims 23-29 and 31 under 35 U.S.C. §101 and §112, first paragraph for alleged lack of utility is respectfully requested.

35 U.S.C. §112, first paragraph- Written Description

Claims 23-29 and 31 are rejected under 35 U.S.C. §112, first paragraph for alleged lack of written description. Specifically, the Patent Office alleges that the "claimed subject matter was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention" [Official Action, Item 10 at page 11, paragraph 4].

As a first point, the claims have been amended herein and are presently drawn to polynucleotides comprising a polynucleotide sequence of SEQ ID NO: 11, polynucleotides comprising a polynucleotide sequence having at least 90% sequence identity to SEQ ID NO: 11, polynucleotides complementary thercto, and RNA equivalents thereof.

A. The Specification Sufficiently Describes the Claimed Invention

In light of the claim amendments provided herein, the Patent Office's allegation that "broadly claimed nucleic acid sequence which encodes a polypeptide which is at least 90% identical to amino acid sequence to SEQ. ID. NO: 5, biologically active fragments or immunogenic fragments of said nucleic acid... are not set forth in the specification" [Official Action, Item 10 at page 12, paragraph 1] is rendered moot.

Applicants respectfully assert that the specification provides sufficient written description for the claimed invention. In fact, the Patent Office itself admits that "an isolated polynucleotide sequence consisting of SEQ ID NO: 11 and an isolated polynucleotide that encodes the polypeptide SEQ. ID. NO: 5 **meet the written description provision** of 35 U.S.C. 112, first paragraph" [emphasis added in bold, Official Action, Item 10 at page 12, paragraph 1].

"Describing the complete chemical structure, i.e., the DNA sequence, of a claimed DNA is one method of satisfying the written description requirement" [Official Gazette, January 30, 2001, "Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, 1 'Written Description' Requirement, quoted from *Eli Lilly*, 119 F.3d at 1156]. In the present case, the specification explicitly describes the complete chemical structure, *e.g.*, the DNA sequence of SEQ ID NO: 11, of the invention. The specification further provides exemplary methods of determining polynucleotides which have 90 % sequence identity to SEQ ID NO: 11, such as the MegAlign™ program [Specification at page 12, lines 26-35], the Jotun Hein method [Specification at page 13, lines 1-2], and varying hybridization conditions [Specification at page 13, lines 3-4]. Therefore, the specification fulfills the written description requirement by providing a complete chemical structure for the claimed invention and exemplary methods by which one of ordinary skill could make the invention.

The Patent Office further alleges that "the specification fails to teach the structure or relevant identifying characteristics of a representative number of species of a representative number of polynucleotides... sufficient to allow one skilled in the art to determine that the

inventor had possession of the invention as claimed" [Official Action, Item 10 at page 13, paragraph 1]. As discussed above, the specification explicitly describes the complete chemical structure, *e.g.* the DNA sequence of SEQ ID NO: 11, of the invention and further provides exemplary methods of determining polynucleotides having 90% sequence identity to SEQ ID NO: 11. Additionally, the specification discusses exemplary methods for selecting polynucleotides that are complementary to SEQ ID NO: 11, such as hybridization assays under varying stringency conditions [Specification at page 18, line 26- page 19, line 23]. Furthermore, the specification discusses exemplary methods for making RNA equivalents of invention polynucleotides, such as *in vitro* transcription by T7, T3, or SP6 RNA polymerases [Specifiation at page 25, lines 11-23].

B. The Specification Sufficiently Describes Inventive Polypeptides

The Patent Office alleges that an inventive protein is "uncharacterized by this specification and is not asserted to belong to any known family of proteins" [Official Action, Item 10 at page 13, paragraph 2]. As detailed in the exemplary citations discussed above in this Response, the specification explicitly describes inventive polypeptides as novel oxidoreductase proteins [Specification at page 5, lines 17-19] and as sharing **"chemical and structural similarity** with sunflower cytochrome b5/desaturase fusion protein" [emphasis added in bold, Specification at page 16, lines 30-31].

For the reasons provided above, Applicants respectfully assert that the present specification conveys to one of skill that Applicants were in possession of the claimed invention. As evidenced by the exemplary citations provided above, the specification explicitly describes distinguishing identifying characteristics of the claimed invention. Accordingly, withdrawal of the rejection of claims 23-29 and 31 under 35 U.S.C. §112, first paragraph for alleged lack of written description is respectfully requested.

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Claim Objections

The Patent Office's objection to claims 23, 24, and 28 as being dependent on non-elected claims 21 and 22 is rendered moot in light of the claim amendments provided herein.

35 U.S.C. §112, first paragraph- Written Description

In light of the claim amendments provided herein, the Patent Office's rejection of claims 23-29 and 31 for alleged indefiniteness is rendered moot. Specifically, the phrases "biologically active fragments" and "naturally occurring amino acid sequence" are not presently recited in the claims.

35 U.S.C. §102- Anticipation

The Patent Office alleges that claims 23-29 and 31 are anticipated by Cho et al. (Journal of Biological Chemistry, Vol. 274: 474-477 (1999)). Applicants respectfully disagree and submit that the disclosure of Cho et al. does not qualify as prior art against the present application. As discussed above in the Response herein, SEQ ID NO: 11 of the present application was disclosed in U.S. Provisional Application 60/155,241, filed on July 16, 1998. Therefore, the present application has an earlier priority date relative to the Cho et al. reference. Applicants respectfully assert that the rejection of claims 23-29 and 31 under 35 U.S.C. §102(a) for alleged anticipation is inappropriate and withdrawal is respectfully requested.

The Patent Office alleges that claims 23-29 and 31 are anticipated by Mukerji et al. (U.S. Patent No. 6,428,990 (filed on November 12, 1999) and U.S. Patent No. 6,432,684 (filed on January 8, 1999)). Applicants respectfully disagree and submit that U.S. Patent Nos. 6,428,990

and 6,432,684 do not qualify as prior art against the present application. As discussed above, the priority date of the present application is earlier than the filing date of U.S. Patent Nos. 6,428,990 and 6,432,684. Therefore, the rejection of claims 23-29 and 31 under 35 U.S.C. §102(e) for alleged anticipation is inappropriate and withdrawal is respectfully requested.

CONCLUSION

In light of the amendments and arguments provided herein, Applicants believe that the present application is now in condition for allowance. Entry of the claims as amended is respectfully requested.

The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 50-0872.

Date July 19, 2004

Respectfully submitted,

By _____

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